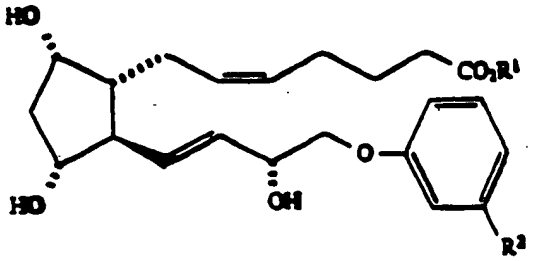
REMARKS

The present invention provides a method of treating glaucoma and ocular hypertension which comprises topically administering to the affected eye a therapeutically effective amount of a compound of formula:



wherein R^1 =hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C_1-C_{12} alkyl cycloalkyl or aryl; and R^2 = Cl_1 or CF_3. (See claim 26.) Topical ophthalmic compositions useful in the method of the invention are also provided. (See claim 34.)

The applicants have added new claims 47 and 48 to specifically claim a method of using fluprostenol for treating glaucoma and ocular hypertension and pharmaceutical compositions useful in said method. (See new claims 47 and 48.) Support for said new claims is found in Example 6, at line 2 of page 18 of the specification.

The Examiner has rejected claims 26, 28-34 and 36-45 under 35 USC § 112, first paragraph, because the specification, while being enabling for R^1 as H, lower alkyl or a cation, does not reasonably provide enablement for applicants' added groups. (By this the Examiner is excluding "a pharmaceutically acceptable amine moiety or...cycloalkyl or aryl" from the definition of R^1.) The Examiner argues that "specification does not enable any person skilled in the art to which it pertains, or with

which it is most clearly connected, to make and/or use the invention commensurate in scope with these claims."

The Examiner has cited as prior art, Bishop et al U.S. Patent 5,510,383 (hereinafter Bishop et al), discussed below, in his rejection under USC § 102(e) and 103(a). The claims of the present application were copied from Bishop et al. In Bishop et al the various ester groups that the Examiner insists are not enabled by applicants' specification are discussed, at from Column 3, line 65 through Column 4, line 9. In Bishop et al, it is made clear that all such ester groups, including cycloalkyl or aryl are made by conventional procedures. For example, at lines 7 and 8 of Column 4 of Bishop et al it is stated that "(s)ince such esterification reactions are well known, they are not further described here." As to the excluded amine moiety, it is believed that such amine is disclosed in Bishop et al as a salt. (See column 3, line 55.) And Bishop et al states that salts can be conventionally formed from the acid form. (See column 3, lines 64 and 65 of Bishop et al wherein, as to the formation of the alkali or alkali metal salts, salt formation is described as conventional.) Thus, clearly Bishop et al, which the Examiner cites as prior art to the applicants' claims 26, 28-34 and 36-45, supports applicants' argument that <u>making</u> compounds with all of the R^1 groups claimed by applicant is within the ordinary skill of the art.

In addition, it is clear that applicant has taught that all of the compounds, wherein R^1 is other than H, lower alkyl or a cation, may be <u>used</u> to treat glaucoma and ocular hypertension. In Examples 6 and 7 a method for evaluating applicants' compounds for such use is disclosed. One of ordinary skill in the art could use the methodology of

Examples 6 and 7 to evaluate any and all of the compounds, having R^1 groups that Examiner argues are not enabled, for treating glaucoma and ocular hypertension.

Thus, it is believed that in accordance with 35 USC § 112, first paragraph, applicants have shown how to make and use the claimed invention commensurate in scope with claims 26, 28-34 and 36-45.

Alternatively, it is not understood how the Examiner can argue that the present claims are not enabled if the prior art asserted by the Examiner, i.e. Bishop et al, with the same disclosure, issued claims that are enabled. (See applicants' argument, as set forth in the previously filed amendments and Appeal Brief, wherein it is pointed out that the claims of the parent of the present application provide support for the claimed subject matter.) Note that Bishop et al in his working Examples shows only the activity of the 1-isopropyl esters of fluprostenol and cloprostenol. The remainder of Bishop et al's disclosure is equivalent of the applicants' disclosure.

(It is noted that claims 27 and 35, wherein R^1 is H, CH_3, $CH(CH_3)_2$ or $C(CH_3)_3$ are not rejected under 35 USC § 112. The significance of this failure to reject claims 27 and 35 under 35 USC § 112 is disclosed below.)

Not withstanding the above argument, it is not understood why the Examiner has rejected claims 42 through 45 under 35 USC § 112, first paragraph, since when R^1 is lower alkyl in claim 1 of Bishop et al and present claim 26, as the Examiner agrees is supported by the present specification, the 1 position of the compound of the formula of said claim 1 of Bishop et al and said claim 26 of the present application, is an ester moiety, as required by applicants' claims 42 through 45. Therefore, the Examiner

is specifically requested to drop his rejection of claims 42 through 45 under 35 USC § 112, first paragraph.

The Examiner has rejected claims 26-45 under 35 USC § 102(e) as being anticipated by Bishop et al. As stated above, claims 26-45 of this application has been copied from U.S. Patent 5,510,383, i.e. Bishop et al, to provoke an interference.

The Examiner argues that contrary to applicants' arguments, the disclosure of U.S. Patent Application 08/605,567, i.e. the parent of the present application, is narrower than the present claims. (It is not understood how this rejection can apply to claims 27 and 35, which the Examiner has not rejected under 35 USC § 112, first paragraph. Moreover, for reasons given above, since claims 42 through 45, are clearly not properly rejected under 35 USC § 112, first paragraph, these claims should not be rejected under 35 USC § 102(e) either.)

The Examiner rejected Claims 26-45 under 35 USC § 102(e) as being anticipated by Bishop et al which discloses and claims the use of cloprostenol, fluprostenol, etc. to treat glaucoma and ocular hypertension. (See the Title of Bishop et al.) The Examiner has previously argued that (t)hese claims are not patentable to the applicant because they are rejected under 35 USC § 112, first paragraph and under 35 USC § 102(e) above, and "an interference cannot be initiated since a prerequisite for interference under 37 CFR § 1.606 is that claims be patentable to the applicant subject to a judgement in the interference." (Note, the Examiner has not rejected claims 27 and 35 under 35 USC § 112, first paragraph, therefore as to these claims, at least, the 35 USC § 102(e) rejection is clearly incorrect. Moreover, even if the Examiner is right

as to claims 26, 28 through 34 and 36 through 41, applicants believe, as argued above, that the Examiner is incorrect in his rejection of claims 42-45 under 35 USC § 112, first paragraph.)

The applicants wish to point out that claims 26 through 45 are supported in the Great-Great Grandparent Application which predates the filing date of Bishop et al as follows and therefore are not properly rejected under 35 USC § 102(e):

It is clear that the applicants disclose in the U.S. Patent Application 948,056, filed on September 21, 1992, from which this application ultimately depends, (hereinafter the "Great-Great Grandparent Application"), the compound 16-m-chlorophenoxy $PGF_{2\alpha}$, i.e. cloprostenol which is the corresponding acid of the isopropyl ester designated as A in Table 1 of Bishop et al. (The acid, i.e. cloprostenol, is included in claim 1 of Bishop et al, i.e. where R^1 is hydrogen and R^2 is chlorine.) This compound is also shown at Table V of the Great-Great Grandparent Application to be an effective IOP lowering agent both as an acid and as the 1-hydroxyl and 1-amido derivative thereof. Note the methyl ester and the amido derivatives of 16-m-chloro phenoxy $PFG_{2\alpha}$, i.e. cloprostenol, are prepared in Examples 8 and 9 of the Great-Great Grandparent Application while the 1-hydroxy derivative is prepared in Example 15 of the Great-Great Grandparent Application.

The applicants also hereby submit a Declaration Under Rule 1.131 which demonstrates that, prior to the filing date of Bishop et al, the applicants had reduced to practice the present invention as related to fluprostenol in the United States. Fluprostenol is the corresponding acid of the isopropyl ester designated as B in Bishop et al and is also

included in claim 1 of Bishop et al, when R^1 is hydrogen and R^2 is CF_3.

Thus, as to the compounds upon which the invention of Bishop et al is based, i.e. cloprostenol and floprostenol, applicants have either an earlier filing date or declaration showing a reduction to practice prior to the filing date of Bishop et al. The further disclosure of Bishop et al, that the acids cloprostenol and fluprostenol may be esterified or converted to a pharmaceutically acceptable salt for the purpose of treating glaucoma or ocular hypertension is obvious in view of applicants' showing of the same activity for said acids in the Great-Great Grandparent application and the Declaration under 37 CFR § 1.131.

Furthermore, applicants believe that under 35 USC § 102(g) Bishop et al's claims aren't patentable since applicants believe that they show that the invention of Bishop et al "was made in this country by another", i.e. Woodward et al prior to the date of invention by Bishop et al. The Declaration under 35 USC § 1.131 is filed to show Woodward et al made the invention before Bishop et al's filing date. The Examiner is referred to Bates v. Coe 98 U.S. 31, 34 (1878) wherein it is stated that "the presumption in respect to the invention described in the patent in suit, if it is accompanied by the application for the same, is that it was made at the time the application was filed; and the complainant or plaintiff may, if he can, introduce proof to show that it was made at a much earlier date."

Thus, for three reasons, the Examiner is incorrect in his rejection under 35 USC § 102(e):

First, the applicants have an earlier filing date than Bishop et al. (This has not been contested by the Examiner in the case of claims 27 and 35.)

Second, applicants are entitled to prove in an interference that they are the prior inventors and entitled to a patent on the invention defined in claims 26 through 45.

Third, the patentees, i.e. Bishop et al, may not be entitled to the patent under 35 USC § 102(g) since they were not the first to make the invention.

Finally, if the Examiner can take the position that in order to provoke an interference an applicant must show support for the claims according to 35 USC § 112, first paragraph, in an application that predates the filing date of a patent, then under U.S. Patent Law the first to file, not the first to invent, will obtain the patent. This is clearly not the law.

The Examiner has rejected claims 26-45 under 35 USC § 103(a) as being unpatentable over Bishop et al. The Examiner argues that "Bishop et al discloses compounds of general formula I to be useful in treating glaucoma and ocular hypertension. In said formula, R^1 may be hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C_1-C_{12} alkyl, cycloalkyl or aryl and R^2 may be chloro or trifluoromethyl. The instant invention differs from the teaching of the cited reference in although generically disclosed, not all of the compounds are specifically exemplified in the reference. It would have been prima facie obvious at the time of the invention was made to one of ordinary skill in the art to start with the teaching of the cited references, to make other of applicants' compounds in view of compounds actually made in

the Bishop et al reference and to expect them to be useful in the treatment of glaucoma and ocular hypertension."

First, the Examiner's rejection under 35 USC § 103(a) is incorrect as it relates to claims 27 and 35 since claims 27 and 35 are not rejected under 35 USC § 112 and therefore predate the filing date of Bishop et al. Second, for the reasons given above, the remaining claims are not properly rejected under 35 USC § 112, first paragraph, and therefore pre date the filing date of Bishop et al and therefore are not properly rejected under 35 USC § 103(a), either.

Claim 46 which defines a method of treating glaucoma and ocular hypertension with cloprostenol is not rejected.

The applicants have added new claims 47 and 48 to claim a method using fluprostenol to treat glaucoma and ocular hypertension and ophthalmic compositions useful in said method.

It is believed that the applicants have now overcome the Examiner's rejections under 35 USC § 112, first paragraph, and 35 USC § 102(e) and § 103(a). The Examiner is hereby requested to declare an interference between the present claims and all of the claims of Bishop et al.

Respectfully submitted,

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